Practitioner's Docket No. MPI98-149P1USRCEM **09/775,803**

REMARKS

In response to the Final Office Action mailed December 15, 2003 (Paper No. 112403), Applicant thanks the Examiner for considering Applicant's arguments and withdrawing the rejection based on 35 USC §103.

Claims 1, 5, 10, 15, 21, 23, and 26-30 have been amended. The term "line" in claims 23, 24, 26, and 27 was deleted for consistency purposes. Support for this amendment can be found at page 8, line 21. The remaining amendments to the claims are described below in sections responding to the Examiner's rejections. Claims 1, 3, 5, 8, 10, 13, 15, 21, 23, 24, and 26-30 are pending. No new matter has been added.

REJECTION OF CLAIMS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1, 3, 5, 8, 10, 13, 15, 21, 23, 24, and 26-30 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected, to make and/or use the full scope of the invention. The Examiner argues that the scope of the claims does not enable one skilled in the art to produce a transgenic mouse with a phenotype described in the specification without undue experimentation. The Applicants produced a mouse which was transgenic for modified GP V gene and which displayed decreased bleeding time. The Examiner cites a publication by Kahn, et al. (1999) Blood 94:4112-4121, who produced a transgenic GP V-deficient mouse and did not observe the phenotype reported by Applicants. The Examiner considers that the construct used by Applicants, wherein a GP V allele is altered to remove Met 1 to Leu 389 of GP V led to the different phenotype from Kahn, et al., who deleted the entire GP V coding sequence. Applicants respectfully traverse this rejection.

Applicants first note that Applicants' construct, which removes at least the initiator methionine and continues through the signal sequence to leucine 389, would, if transcription of the remainder of the GP V gene were to occur, produce an RNA which would be expected not to be able to produce a protein presentable extracellularly, if such an RNA would not be degraded. In confirmation of this possibility, Applicants, using an antibody which recognizes amino acid sequences (amino acids 432-450 and 472-490, page 13, lines 13-14) encoded by the retained portion of GP V, did not detect GP V on the platelet surface by FACS or in lysates by Western blotting (page 21, lines 21-24). This result was observed even though the normal complex companions of GP V, GP Ib and GP IX, were detected at normal levels on the cell surface.

The Examiner also was not convinced by Applicants' arguments regarding differences in the observations made by Applicants and Kahn et al.. The Examiner believes that the last response (from 9/16/03) had statements which appear to conflict with statements in a response from 5/30/02. The Examiner asks for clarification. Applicants note that the 5/30/02 statements spoke of "different reagents

and methodologies" and the 9/30/02 response discussed, for example, differences in statistical analysis of results. One skilled in the art would recognize statistical analysis as a pursuit governed by methodology. Therefore, the Applicants' use of methods which included statistical analysis of bleeding time is a difference in methodology from Kahn et al., who did not use statistical methodology to conclude their result. In the 9/16/03 response, Applicants also noted further differences in methodologies by noting the ATP secretion method, fibrinogen binding method, and lumiaggregometry *versus* flow cytometry to test platelet activation. Applicants believe the 9/16/03 response did not conflict with the 5/30/02 response, rather, the 9/16/03 response just included further elaboration.

Nevertheless, in the interest in furthering prosecution of this application, Applicants have replaced protein structure and protein effect language in claims 1, 5, 10, 15, 21, 23, and 28-30 (claims 3, 8, 13, 24, 26 and 27 dependent thereon) by construct structure and genomic effect language. This construct structure language recites a deletion of GP V nucleotides encoding Met 1 to Leu 389 and genomic effect language describes that the modification be at an allele of GP V. Support for these amendments can be found in the specification at page 8, lines 1-2 and page 14, lines 22-23. In view of these amendments and for the reasons put forth above, Applicants request that this rejection be withdrawn.

REJECTION OF CLAIMS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1, 3, 5, 8, 10, 13, 15, 21, 23, 24, and 26-30 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner rejected these claims for omitting essential structural cooperative relationships of elements when reciting decreased bleeding time. Applicants respectfully traverse this rejection.

Applicants have amended claims 1, 5, 10, 15, 21, 23, and 28-30 (claims 3, 8, 13, 24, 26 and 27 dependent thereon) to recite that the comparison is to a mouse homozygous for wild type GP V. In view of these amendments, Applicants request that this rejection be withdrawn.

The Examiner further rejected claims 5, 8, 10 and 13 for the presence of the phenotype in the preamble of those claims. In response, Applicants have moved the bleeding time comparison into the body of the steps of the methods in claims 5 and 10 (claims 8 and 13 dependent thereon). In view of these amendments, Applicants request that this rejection be withdrawn.

CONCLUSIONS

Applicants respectfully request that the Examiner enter these amendments after final rejection because, in view of these amendments and remarks, Applicants respectfully submit that the rejections of

claims 1, 3, 5, 8, 10, 13, 15, 21, 23, 24, and 26-30 under 35 U.S.C. §112 are herein overcome and that this application is now in condition for allowance. Early notice to this effect is solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned. If the Examiner disapproves of Applicant's amendments and remarks in this response, Applicant requests a prompt mailing of an Advisory Action to that effect.

This paper is being filed timely within three months of the mailing date of the final action. No extensions of time are required. In the event any extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

February 26, 2004

Respectfully submitted,

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